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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,796	12/08/2006	Jay D. Keasling	B03-097-2 (BERK-032)	7712
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UC Berkeley - OTL Bozicevic, Field & Francis LLP 1900 University Avenue, Suite 200 East Palo Alto, CA 94303			EXAMINER VOGEL, NANCY TREPTOW	
			ART UNIT	PAPER NUMBER
			1636	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/573,796	Applicant(s) KEASLING ET AL.	
	Examiner NANCY VOGEL	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-63 is/are pending in the application.
- 4a) Of the above claim(s) 41-61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-29, 39, 40, 62 and 63 is/are rejected.
- 7) ☒ Claim(s) 30-38 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/4/09, 3/8/07</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims 1-63 are pending.

Receipt of the Information Disclosure Statements on 6/4/09 and 3/8/07 is acknowledged.

Election/Restrictions

Applicant's election of Group I, species 1) source of exogenous nucleic acid, prokaryotic cell; 2) host cell, prokaryotic cell; 3) biosynthetic pathway, mevalonate kinase, phosphomevalonate kinase, mevalonate pyrophosphate decarboxylase, and isopentenyl pyrophosphate isomerase; 4) product encoded by the nucleic acid with which the genetically modified host cell is genetically modified, a terpene biosynthetic pathway intermediate-modifying gene product; in the reply filed on 4/17/09, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Sequence compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences are set forth in the specification and drawings that lack sequence identifiers. (See Fig. 12, It is often convenient to identify sequences

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in figures by amending the Brief Description of the Drawings section (see MPEP 244.02). If the sequences are already present in the sequence listing, it would be remedial to amend the Brief Description of the Drawings to include the appropriate sequence identifiers. Applicants are required to comply with all of the requirements of 37 CFR 1.821 - 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F. R. 1.821 through 1.825 did not preclude the examination of the application on the merits, the results of which are communicated below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20, 39, 40, 62, 63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

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To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that “the inventor invented the claimed invention.” *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (“[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.”). Thus, an applicant complies with the written description requirement “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.” *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

A written description of an invention involving a chemical genus, like a description of a chemical species, “requires a precise definition, such as by structure, formula, [or] chemical name,” of the claimed subject matter sufficient to distinguish it from other materials. *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) (“In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...”) *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is “not a sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.” MPEP § 2163.

The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass

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the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include: (1) Actual reduction to practice, (2) Disclosure of drawings or structural chemical formulas, (3) Sufficient relevant identifying characteristics (such as: i. Complete structure, ii. Partial structure, iii. Physical and/or chemical properties, iv. Functional characteristics when coupled with a known or disclosed, and correlation between function and structure), (4) Method of making the claimed invention, (5) Level of skill and knowledge in the art, and (6) Predictability in the art.

“Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.” MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a genus of methods in which a genetically modified host cell is used, which is genetically modified such that a

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biosynthetic pathway intermediate is produced in an amount effective to inhibit growth of the genetically modified host cell.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1-20, 39, 40, 62, 63 are broad and generic, with respect to all possible cells comprise genetic modifications that result in the production of a biosynthetic pathway intermediate in an amount effective to inhibit growth of the genetically modified host cell encompassed by the claims. The possible structural variations are numerous since there is no structural requirement recited. Therefore, any host cell comprising any alteration resulting in the recited property of having an intermediate produced in an amount to inhibit growth, is encompassed.

Specifically, the claims lack written description because although one of ordinary skill in the art could reasonably predict the genetic modifications in any particular host cell which would result in the product of an intermediate in a biosynthetic pathway that would inhibit growth of the cell. One could not reasonably predict intermediates which would have the effect, at any level of production, of growth inhibition. It is clear that experimentation would be required to determine whether any particular host cell, having modifications in any particular gene, producing any particular intermediate, at any particular level of production, would meet the functional requirement.

Therefore, one of ordinary skill in the art would not be able to determine which of the species of biosynthetic intermediates, produced in any particular amount, would have growth inhibition activity without experimentation and thus the structure-function

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correlation is considered to be unpredictable. Although the claims recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. The specification does not provide a representative number of examples of such biosynthetic intermediates, since the only examples are drawn from the biosynthetic pathway for terpene biosynthetic pathways wherein the intermediate is a prenyl disphosphate.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does “little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.”) Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5, 11-15, 21-29 are rejected under 35 U.S.C. 102(a) as being anticipated by Martin et al. (Nature Biotechnology, 21, 7, 796-802, July 2003)(cited by applicants).

Martin et al. disclose a method comprising producing a test cell by introducing into a genetically modified host cell, and exogenous nucleic acid comprising a nucleotide sequence encoding a candidate gene product, wherein the genetically modified host cell produces a biosynthetic pathway intermediate, which intermediate is produced in an amount effective to inhibit growth of the genetically modified host cell; and determining the effect on growth of the test cell (see page 797, first column, first paragraph; see page 800, right column, last paragraph). The genetically modified host cell is genetically modified with nucleic acids encoding one or more of acetoacetyl-CoA thiolase, HMG-CoA synthase, mevalonate kinase, phosphomevalonate kinase, mevalonate pyrophosphate decarboxylase, isopentenyl pyrophosphate isomerase, (Fig. 1). The genetically modified host cell is cultured in the presence of mevalonate (see page 797, left column, last paragraph).

Claims 30-38 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

NV
6/17/09